PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : G01N 27/447	A1	(11) International Publication Number: WO 00/22427 (43) International Publication Date: 20 April 2000 (20.04.00)

(21) International Application Number: PCT/NL99/00641

(22) International Filing Date: 15 October 1999 (15.10.99)

(30) Priority Data:
1010327 15 October 1998 (15.10.98) NL

(71) Applicant (*for all designated States except US*): UNIVERSITEIT TWENTE [NL/NL]; Mesa Research Instituut, Drienerlolaan 5, NL-7522 NB Enschede (NL).

(72) Inventor; and
(75) Inventor/Applicant (*for US only*): VAN DEN BERG, Albert [NL/NL]; Eversbergweg 3, NL-7443 PC Nijverdal (NL).

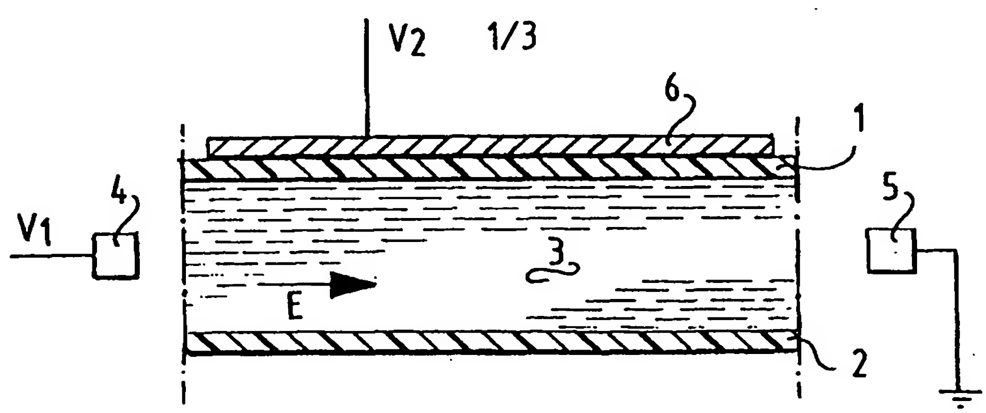
(74) Agent: LAND, Addick, Adrianus, Gosling; Sweelinckplein 1, NL-2517 GK The Hague (NL).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.
In English translation (filed in Dutch).

(54) Title: DEVICE AND METHOD FOR CONTROLLING A LIQUID FLOW



(57) Abstract

The present invention relates to a device for controlling a liquid flow in a liquid channel, comprising: an elongate liquid holder in which a liquid channel is provided in longitudinal direction; first voltage means for applying a first voltage difference over substantially the longitudinal direction of the liquid channel; a conductor member arranged in at least a part of the liquid channel against the liquid holder; an insulator member arranged in the liquid channel against at least the conductor member; second voltage means for providing a second voltage difference between the conductor member and the liquid in the liquid channel; wherein the thickness of the insulator member is a maximum of 1 μm and preferably in the order of magnitude of some tens of nanometres.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

DEVICE AND METHOD FOR CONTROLLING A LIQUID FLOW

The present invention relates to a device for controlling a liquid flow in a liquid channel. The present invention also relates to an assembly and integrated circuit in which this device is placed, and to a method for manufacture thereof.

Charged particles in a solution or suspension of a liquid channel can be transported by applying an electric field substantially parallel to the liquid channel. Under the influence of the electric field positively and negatively charged particles will move in opposing directions. This transport is also referred to as electrophoresis.

Another mechanism for generating a liquid flow in a liquid channel is formed by so-called electro-osmosis. The liquid channel is in this case enclosed by an electric insulator. At the location of the transition between the insulator and the liquid are situated charged insulator particles which are chemically bound to the insulator. As a consequence of the charge of these insulator particles, particles with an opposing charge are formed close to the insulator wall in the liquid channel. The layer consisting of the chemically bound insulator particles and the liquid particles charged in opposing directions is also referred to as the electric double layer. As a result of the presence of these particles with opposing charge, which are not chemically bound to the insulator, and the above mentioned electric field applied parallel to the direction of the liquid channel, a liquid flow will be generated along the walls of the liquid channel. The liquid flow along the walls brings about a liquid flow across the entire diameter of the liquid channel as a result of the friction between the liquid particles.

The moving charged particles define a shear plane at some distance of the insulator wall. The electrical potential at the location of this shear plane is called the ζ-potential (Zeta potential). The magnitude of the ζ-potential depends inter alia on factors such as the type of liquid or insulator, the concentrations of the different particles in the liquid, the pH value and the like. The direction and the degree of liquid flow resulting from electro-osmosis can be controlled by changing these factors.

It can be deemed known to vary the potential of the outer surface of the insulator with a voltage source, as a result of which the above stated ζ-potential in the liquid channel can be varied. Since the direction and speed of the liquid flow in the liquid channel depends on the magnitude of the ζ-potential, the movement of the particles in the liquid can be controlled with the voltage source, i.e. the movement of particles resulting from electrophoresis can be enhanced or decreased. While there are indeed devices known which enable such a control of the liquid flow in a liquid channel, they have large dimensions and require very high control voltages in the order of magnitude of several kVs, so that in practice they cannot be integrated with standard electronic components such as transistors, integrated circuits and so on.

The object of the present invention is to obviate these drawbacks.

According to an aspect of the invention, a device is provided for this purpose for controlling a liquid flow in a liquid channel, comprising:

- an elongate liquid holder in which a liquid channel is provided in longitudinal direction;
- first voltage means for applying a first voltage difference over substantially the longitudinal direction of the liquid channel;
- a conductor member arranged in at least a part of the liquid channel against the liquid holder;

- an insulator member arranged in the liquid channel against at least the conductor member;

- second voltage means for providing a second voltage difference between the conductor member and the liquid in the liquid channel;

wherein the thickness of the insulator member is a maximum of 1 μm and preferably in the order of magnitude of some tens of nanometres. In accordance with this aspect of the invention a device is therefore provided for controlling a liquid flow, wherein the functions of liquid container or liquid holder on the one hand and of insulator or ζ-potential control layer on the other are separated, so that a great flexibility can be achieved in choice of material and method of manufacture.

According to a preferred embodiment of the invention the insulator member is formed from a thin layer or coating of insulator material, the conductor member and the liquid holder are combined and formed from a mechanically stable conductor material. The mechanically stable material provides in this case the required sturdiness of the device.

According to a further preferred embodiment of the invention the insulator member and the conductor member are formed from thin layers of respectively insulator material and conductor material, wherein the liquid holder is preferably formed from a mechanically stable material.

According to another aspect of the invention, a device is provided for controlling the liquid flow in a liquid channel, comprising:

- an insulator member which defines an elongate liquid channel;

- first voltage means for applying a first voltage difference over substantially the longitudinal direction of the liquid channel;

- a conductor member arranged over at least a part of the outer surface of the insulator member;

- second voltage means for providing a second voltage difference between the conductor member and the liquid in the liquid channel;

wherein the distance between the outer surface and the inner surface of the insulator member is a maximum of 1 μm and preferably in the order of magnitude of some tens of nanometres. By making the wall thickness of the insulator member so small, the control of the liquid flow can advantageously be performed with a small second voltage difference, for instance with a voltage difference of less than 20 Volt. At such small wall thicknesses there moreover occurs a reduced loss of power and an improved heat discharge is possible.

According to a further preferred embodiment of the invention the device can be directly connected to standard electronic elements or integrated circuits or can even be integrated therewith. This preferred embodiment can therefore be advantageously connected directly onto and controlled by the output of the standard electronic elements such as integrated circuits, without additional provisions being required therein.

According to a further preferred embodiment of the invention the insulator member and the conductor member are manufactured from optically transparent materials. This has the advantage that the content and/or composition of the content of the liquid channel can be optically detected in simple manner.

According to a further preferred embodiment of the invention the insulator member is constructed from two or more insulator part-members manufactured with materials of different ζ-potential. This has the advantage that various flows with differing speeds and directions can be generated in the liquid channel without applying an external potential difference.

According to a further embodiment of the invention the insulator member is provided with two or more conductor members, to which mutually differing voltages can be applied. By applying different potentials

to the conductor members, the associated ζ-potentials in the liquid channel will accordingly differ from each other. This has the advantage that different flows with differing speeds and/or directions of movement can be generated within the same liquid channel.

According to another preferred embodiment the voltage means comprise two electrodes which are arranged in the liquid channel. Because the electrodes can be arranged in the liquid the distance between the electrodes can be reduced, at least relative to the distance in the case of external electrodes, to an order of magnitude of a few micrometers. Lower voltages are hereby sufficient to obtain the desired field strength of the electric field.

According to a further aspect of the invention, a system is provided for analysis and/or synthesis of chemical solutions or suspensions, wherein one or more of the above stated devices is used. According to a preferred embodiment of this system, this system comprises control means for controlling one or more liquids through a network of said devices.

According to a further preferred embodiment the network of said devices comprises one or more feed channels, two intermediate channels branched from the feed channels and one or more drain channels connected to the intermediate channels, wherein the intermediate channels are provided with gates which are supplied with voltage such that in the intermediate channels a substantially loop-like liquid flow results. Using such loop-like liquid flows the liquid in the intermediate channels can be circulated so that the liquid is mixed or enters into a chemical reaction.

According to a further aspect of the present invention, a pump system is provided for circulating liquid, in which preferably one or more of the above stated devices are used, comprising:

- a liquid holder in which are provided a liquid feed channel and a liquid drain channel branched from the liquid feed channel;

- first voltage means for applying an electric field in the longitudinal direction of the liquid feed channel;

- a first and a second gate electrode which are placed on either side of the connection of the liquid drain channel to the liquid feed channel;

- second voltage means for providing the first and second gate electrode with voltage;

- control means for adjusting the first and second voltage means such that a pressure build-up occurs at the location of said connection and the liquid is drained via the liquid drain channel.

With the above stated system a pump can be realized on micro-scale, wherein the drain channel of the pump is voltage-free, this being advantageous since the drain channel can thereby be connected more easily to peripheral equipment and the like.

According to further embodiments of the above stated pump system, the first voltage means generate an electric field alternately in a first and in a second opposing direction in the liquid feed channel and the second voltage means, substantially synchronously with the first voltage means, switch the first gate electrode into enhancement mode and the second gate electrode into a reversement mode and vice versa. By circulating the liquid in such a manner polarization effects, such as the creation of air bubbles as a result of electrolysis, do not occur, which polarization effects could have an adverse effect on the operation of the pump.

According to a further aspect of the present invention, an electronic circuit is provided into which the above stated device is integrated.

According to a further aspect of the invention a method is provided for manufacturing the above stated device, comprising of:

- etching a channel in a wafer;
- depositing insulating material on the wafer;
- manufacturing a glass plate;
- anodic binding of the wafer on the glass plate;
- etching the wafer; and
- fixing the conductor member.

By manufacturing the device in this manner liquid channels with the correct properties and very small wall thicknesses of a few tens of nanometres can be realized.

According to a further aspect of the present invention a method is provided for mixing two or more liquids, comprising of:

- supplying the liquids via one or more liquid channels;
- mixing the liquids by circulating the supplied liquid, preferably in the above stated system;
- draining the liquids via one or more liquid drain channels.

Further embodiments, advantages, features and details of the present invention will be elucidated in the following description with reference to the annexed figures, in which:

- figure 1 shows a longitudinal section of a preferred embodiment of the invention;
- figure 2a and 2b show schematic sketches of the operation of the electro-osmosis and electrophoresis mechanisms;
- figure 3 is a schematic perspective view of another preferred embodiment of the invention, in which a network of liquid channels forms an electrical switch;
- figure 4 shows a schematic perspective view of another preferred embodiment of the invention, depicting another electrical switch;
- figure 5 shows a longitudinal section of another preferred embodiment of the invention;

- figure 6 shows a schematic view of a further preferred embodiment of the invention for applications in a bioreactor;
- figure 7 shows a schematic view of a further preferred embodiment for applications in a bioreactor;
- figure 8 is a schematic view of a further preferred embodiment for applications as pump; and
- figure 9a and 9b are schematic views of another preferred embodiment of a pump.

Shown in the longitudinal section of figure 1 is a channel of rectangular cross-section, with an upper wall 1 and a lower wall 2 between which flows a liquid 3. Placed on the left-hand side of the channel is an anode 4 which is set to a voltage of V_1. Placed on the right-hand side of the liquid channel is a cathode 5 which is connected to the earth potential. As a result of the voltage difference between anode 4 and cathode 5 an electric field E is generated which transports positively charged particles in the direction of the arrow shown in the figure and negatively charged particles in the opposite direction (electrophoresis). The presence of positively or negatively charged particles in the liquid channel can be controlled by the choice of the insulator material of the insulator, the pH value of liquid 3, the concentration of the particles in the solution or suspension and so on. The presence of positively or negatively charged particles in the electrical double layer can however also be controlled using a conductor 6 which is arranged on the outside of insulator wall 1 and set to a voltage V_2.

Figure 2a shows the progression of the positive voltage applied to the insulator wall by conductor 6. On the interface 7 between conductor 6 and wall 1 the voltage equals V_2, while the voltage decreases as the interface between wall 1 and liquid 3 is approached. At the location of interface 8 the voltage has a value ψ_0, which voltage is designated as the wall potential. The wall potential is the consequence of charged particles 9,

in this case positively charged particles, chemically bound to wall 1. Negatively charged particles 10 will occur in the liquid to compensate herefor. The voltage in the liquid channel decreases further as the distance from interface 8 increases. As a result of the applied field E the non-bound negatively charged particles 10 will be subjected to a force in the direction of the arrow a. This electric force decreases as the distance from the wall surface increases, since the number of negatively charged particles in this direction decreases. As a result of this electric force the part of the liquid in the electric double layer to the left of the shear plane or inner Helmholtz plane 11 will therefore start to move parallel to the wall surface, while the remaining part of the liquid is co-displaced by friction.

Shown in figure 2b is the situation where the voltage V_2 on conductor 6 is negative, so that the wall potential ψ_0 is negative. There therefore results in the electric double layer, in addition to the chemically bound negative charges 12, a quantity of positively charged particles 13 which are transported in the direction of arrow b as a result of the electric field $\bar{E}$ which is present.

The liquid channels can be manufactured according to a method as described in the article "Glass channels and capillary injectors for capillary zone electrophoresis", pages 77-84, Y. Fintschenko et al, in: A van de Berg en P. Bergveld, "Sensor Technology in the Netherlands: State of the Art", Kluwer Academic Publishers, Dordrecht, 1998, pages 77-84. As alternative to this method of manufacture the devices according to the invention can be manufactured with a so-called "Self-Assembled Mono-layer" (SAM layer) on gold, silver or Si. A monolayer of thioalkanes for instance (which form a very good and thin insulator) is herein coated from the inside on a hollow Au pipe. A sulphur group S is herein bound on the inside of the Au pipe in chemical manner, which group is connected via hydrophobic hydrocarbon

chains to a functional end group, which end group influences the ζ-potential. The total thickness of the SAM layer is about 0.5-10 nm. Alternative manufacturing methods can also be envisaged in addition to the above described methods of manufacture.

By in any case embodying the liquid channels in this manner very thin wall thicknesses of less than 1 μm, preferably in the order of magnitude of a few (tens of) nanometres can be realized. As a result of these small dimensions the required magnitude of the control voltage V_2 is very low, for instance a few mV or V, and generally a maximum of 20 Volt. It is hereby possible to influence the liquid flow with relatively low voltages, wherein use can therefore be made in practice of the voltages occurring in standard electronic components such as transistors, integrated circuits and so on. An improved heat discharge can also be realized due to the small wall thickness. Relative to known liquid channels, which have a wall thickness of about 100 μm, the heat discharge is for instance up to four times faster.

Figure 3 shows a view of a preferred embodiment of the invention, in which an electrical switch is formed in a network of liquid channels. A liquid channel 14 branches at a given position into two liquid channels 15 and 16. Between the beginning of liquid channel 14 and the ends of liquid channels 15 and 16 a potential difference is applied by means of an anode 20 and two cathodes 21 and 22. As a result of this voltage difference a flow occurs in liquid channel 14 in the direction of the arrow shown in figure 3. In order to create an electrical switch with which the flow can be divided over the two liquid channels 15 and 16 at the branching, a conductor 17 is arranged on liquid channel 14, a conductor 18 on liquid channel 15 and a conductor 19 on a liquid channel 16. By supplying conductors 17, 18 and 19 with suitable voltages, the associated potentials are adjusted and the liquid flow in the network of channels can be controlled. Shown in table I is an

overview of the voltage values required to control the direction of the liquid flow. This shows that for flow from channel 14 to channel 15 the voltage V_{17} on conductor 14 must be positive, the voltage V_{18} on conductor 15 must be positive and the voltage V_{19} on conductor 16 must be negative. For flow from channel 14 to channel 16 the voltage V_{17} on conductor 14 must be positive, the voltage V_{18} on conductor 15 must be negative and the voltage V_{19} on conductor 16 must be positive.

TABLE I

	14 → 15	14 → 16
V_{17}	+	+
V_{18}	+	-
V_{19}	-	+

Figure 4 shows an alternative electrical switch wherein the infeed consists of a channel 23 and a channel 24 and the outfeed consists of a channel 25, which either transports the liquid out of channel 23 or the liquid out of channel 24. Anodes 29 and 30 are placed at the beginning of liquid channels 23 and 24, while a cathode 31 is placed at the end of liquid channel 25. By applying a voltage difference hereover an electric field is created in the liquid. Conductors 26 and 27 are moreover arranged on respectively liquid channel 23 and liquid channel 24 and a conductor 28 is arranged on liquid channel 25. Table II shows the voltage values required to control the direction of the liquid flows. This shows that when the liquid flow of channel 23 has to be drained via channel 25, the voltage V_{26} on conductor 26 must be positive, the voltage V_{27} on conductor 27 must be negative and the voltage V_{25} on conductor 25 must be positive. If on the other hand the liquid from liquid channel 24 must be drained through liquid channel 25, the voltage V_{26} on

conductor 26 must be negative, the voltage V_{27} on conductor 27 must be positive and the voltage V_{28} on conductor 28 must be positive.

TABLE II

	23 → 25	24 → 25
V_{26}	+	-
V_{27}	-	+
V_{28}	+ -	+

Figures 3 and 4 show that conductors 17, 18, 19, 26, 27, 28 are preferably connected to a central control 40 in order to control the direction and speed of the liquid flows in the network of liquid channels.

In an embodiment of the invention which is not shown, a large number of electrical switches according to figures 3 and 4 connected in parallel or in series can be combined to an extensive network of liquid channels in which the flow of the liquid can be regulated by a central control.

Figure 5 shows a liquid channel wherein on the upper side of the channel the insulator 32 is manufactured from a first material, while on the underside the insulator 33 is manufactured from a second material, wherein the first and second materials have different ζ-potentials. It is also possible to arrange a conductor 34 on the top side of insulator 32, while a second conductor 35 is arranged against the underside of the bottom insulator 31. If different voltage values are applied to conductors 34 and 35, different ζ-potentials occur in the liquid. When the voltage on conductor 34 is for instance positive, while the voltage on conductor 35 is negative, the liquid in the vicinity of the upper wall will move in the direction of arrow C and the liquid in the vicinity of the bottom wall will move in the

direction of arrow D. It is hereby possible to bring about different directions of movement of the liquid in one channel, which may for instance be important when separating compositions.

The most important field of application of the present invention is in the development of new medicines and bio-analysis. Large numbers of substances must herein be analyzed very quickly, at a speed of for instance more than 10,000 analyses per hour. Another important field of application of the present invention is so-called "fluid-chemical computing" or "DNA-computing", as for instance described in "Computing with DNA" by L.M. Adleman, Scientific American, August 1998, page 34-41. A determined liquid volume in the liquid channel according to the invention, for instance with dimensions of 10 μm*1 μm*1 μm, can easily contain 10^3 DNA molecules, or 10^{12} bits of information. Control of the liquid flow in the liquid channel as set out above with a switching time of 1 μs yields a data transfer speed of 10^{18} bits/s, which is much faster than the data transfer speed in the present electronics.

Figure 6 shows a schematic view of an application of the invention on a pump for circulating and mixing liquids in bioreactor applications. Use is made herein of a circuit of two flow channels in a so-called twin channel network. Figure 6 shows that a liquid is fed via channel 41, which channel 41 subsequently branches into a channel 42 and a channel 43. Channels 42 and 43 join together again a little further along in drain channel 44. Using anode 45 and cathode 46 an electric field, which in the example of figure 6 is directed substantially from left to right, is generated in the channels. Liquid channels 41, 42 and 43 are respectively provided with conductors 47, 48 and 49. Using conductor 47 the liquid is fed in a manner already described with reference to figure 3. By then providing conductors 48 and 49 with suitable voltages, i.e. conductor 48 such that an enhancement mode is generated

and conductor 49 such that a reversement mode is generated, the liquid in liquid channels 42 and 43 is circulated in a clockwise direction, which is indicated in the figure with an arrow. By providing conductors (gates) 48 and 49 with voltage such that in channel 42 the reversement mode and in channel 43 the enhancement mode prevails, the rotation direction of the liquid flow can be reversed. With above stated (twin channel) network liquids can be fed in simple manner and subsequently mixed during circulation. It is also possible to have different liquids react with each other during circulation. Control of gates 48 and 49 (and 47) preferably takes place by means of a central control 40 so that the direction and speed of the liquid flows in the network of liquid channels is easy to control. After the liquid has been circulated sufficiently, gates 48 and 49 are both switched into the enhancement mode whereby the liquid can be drained via liquid channel 44. It is noted that the above stated circulation can also be implemented in other ways. Conductor 47 for instance may thus be omitted as the case requires, or an extra conductor may be added in drain channel 44. It is also possible to place anode and cathode 45 and 47 at other positions or to provide each conductor (gate) 47, 48, 49 with its own anode-cathode pair, for instance in a manner as occurs in a preferred embodiment discussed hereinbelow.

Figure 7 shows another advantageous embodiment, in which liquid is fed via two different liquid channels 51 and 55 into a twin channel network consisting of an upper liquid channel 52 and a lower liquid channel 53, and the liquid is drained in drain channel 54 in a manner corresponding wholly with the embodiments of figure 6. Using anodes 56 and 57 and cathode 58 an electric field is generated in the channel system. Through a suitable switching of gates 59, 60, 61 and 62 associated with respective liquid channels 51, 55, 52 and 53, the different liquids can be fed via the associated feed

channels 51 and 55 in adjustable ratios and can be mixed with each other through being pumped round in channels 52 and 53, wherein a chemical reaction may occur. When for instance a first component is fed via liquid channels 51 and a second component via liquid channel 55, a reaction between the two components can take place during pumping of the two liquids round liquid channels 52 and 53. Depending on the set voltages, the mixing ratio of substances fed via channel 51 and channel 55 can be adapted as desired. At a desired moment, for instance when a reaction between the two liquids has ended, the liquids which have reacted with each other are drained via drain channel 54. also referred to as drain. The above stated mixing ration depends on the feeding speeds in liquid channels 51 and 55 and the volumes in the channels. In addition to being used for a continuous supply of different liquids, the network can also be used in applications in which processes have to be performed batchwise.

It is noted that additional branches of the twin channel network can be connected as desired in order to allow further different components into the circuit.

It is important to adjust the voltages on the gates such that the maximum circulation takes place while the hold-up, i.e. the mixing ratio between the liquids, is optimal.

Figures 9a and 9b show another embodiment of a pump. Figure 9a shows in schematic manner a channel 80 which is provided with the branch 83. Channel 80 is provided with a gate 81 and a gate 82. In a manner as described in the foregoing embodiments, an electric field is generated in channel 80 in the direction of the double arrow. By switching gate 81 into the enhancement mode E and gate 82 into the reversement mode R, a pressure build-up is created in channel 80 such that the liquid is carried into the side channel 83 and is drained via this side channel. The advantage of this manner of pumping is that no electric field is hereby present in channel 83,

or channel 83 is hereby voltage-free. As a result hereof the drain of such a pump can be connected more easily onto external equipment.

Figure 9b shows a situation in which a similar pumping action is brought about in side branch 83, with the difference that the electric field is now directed from bottom to top and gates 81 and 82 are switched in opposing directions, i.e. gate 81 is switched into the reversement mode R and gate 82 into the enhancement mode E. In this configuration the liquid from above is also urged via tube 80 into side tube 83 whereby the channel system functions as pump. By now alternating the situations shown in figures 9a and 9b with a suitable frequency, i.e. reversing the electric field and reversing the switching mode of gates 81 and 82, no polarization effects will occur on the electrodes in the case of a substantially continuous pumping action. The term "polarization effects" refers to the adverse effects which can for instance cause electrolysis in water, whereby gas bubbles occur in the liquid channels and the pumping action is greatly reduced.

Figure 8 shows a further preferred embodiment of a pump. Channel 70 is provided with a gate electrode 73. Arranged on either side of gate electrodes 73 are metal electrodes 71 and 72 with which an electric field can be generated. By applying the electric field between electrodes 71 and 72 an electro-osmotic flow can be created which is influenced by the voltage of gate electrode 73.

By providing electrodes 71 and 72 with alternating voltage there would indeed be no occurrence of polarization effects such as formation of gas bubbles if the voltage of gate electrodes 73 remained constant, but the liquid in the channel is not displaced either. By also switching gate electrode 73 substantially synchronously with alternating of the voltage of electrodes 71 and 72, a liquid flow can still be

generated in channel 70 without polarization effects occurring.

In this embodiment the gate electrodes 71 and 72 are integrated in the tube and (external) electrodes outside the channel can be omitted. This not only has the advantage that such a channel 70 can be connected directly onto external peripherals, but also has the advantage that much lower voltages can be used since the distance d between electrodes 71 and 72 can be much smaller than in the case where the electrodes are arranged externally. Since the distance d is in the order of magnitude of a few micrometers, a pump of extremely small dimensions can be realized.

The above stated invention can be applied not only on aqueous media but also on non-aqueous media such as for instance alcohol, methanol, THF, DMSO or any other random solvents. It may be necessary herein to dissolve organic salts in the medium to ensure a sufficient degree of conductivity.

The present invention is not limited to the above described preferred embodiment thereof; the rights sought are defined by the following claims, within the scope of which many modifications can be envisaged.

CLAIMS

1. Device for controlling a liquid flow in a liquid channel, comprising:

- an elongate liquid holder in which a liquid channel is provided in longitudinal direction;

- first voltage means for applying a first voltage difference over substantially the longitudinal direction of the liquid channel;

- a conductor member arranged in at least a part of the liquid channel against the liquid holder;

- an insulator member arranged in the liquid channel against at least the conductor member;

- second voltage means for providing a second voltage difference between the conductor member and the liquid in the liquid channel;

wherein the thickness of the insulator member is a maximum of 1 μm and preferably in the order of magnitude of some tens of nanometres.

2. Device as claimed in claim 1, wherein the insulator member is formed from a thin layer of insulator material, the conductor member and the liquid holder are combined and formed from a mechanically stable conductor material.

3. Device as claimed in claim 1, wherein the insulator member and the conductor member are formed from thin layers of respectively insulation material and conductor material.

4. Device as claimed in claim 3, wherein the liquid holder is formed from mechanically stable material.

5. Device for controlling the liquid flow in a liquid channel, comprising:

- an insulator member which defines an elongate liquid channel;

- first voltage means for applying a first voltage difference over substantially the longitudinal direction of the liquid channel;

- a conductor member arranged over at least a part of the outer surface of the insulator member;

- second voltage means for providing a second voltage difference between the conductor member and the liquid in the liquid channel;

wherein the distance between the outer surface and the inner surface of the insulator member is a maximum of 1 μm and preferably in the order of magnitude of some tens of nanometres.

6. Device as claimed in any of the claims 1-5, wherein the second voltage difference is a maximum of 20 V.

7. Device as claimed in any of the claims 1-6, wherein it can be directly connected to standard electronic elements or integrated circuits.

8. Device as claimed in any of the claims 1-7, wherein the insulator member and the conductor member are manufactured from optically transparent materials.

9. Device as claimed in any of the foregoing claims, wherein the insulator member is constructed from two or more insulator part-members with different Zeta potential.

10. Device as claimed in any of the foregoing claims,-wherein two or more conductor members, to which differing voltages can be applied, are fixed to an insulator member.

11. Device as claimed in any of the foregoing claims, wherein the liquid channel has a substantially rectangular cross-section.

12. Device as claimed in any of the claims 1-10, wherein the liquid channel has a substantially round or semi-round cross-section.

13. Device as claimed in any of the foregoing claims, wherein the first voltage means comprise two electrodes which are arranged in the liquid channel.

14. Device as claimed in claim 13, wherein the distance d between the electrodes is in the order of magnitude of a few micrometers.

15. System for analysis and/or synthesis of chemical solutions or suspensions, wherein one or more of the devices as claimed in any of the claims 1-14 is used.

16. System as claimed in claim 16, comprising control means for controlling one or more liquid flows through a network of said devices.

17. System as claimed in claim 15 or 16, wherein the network of said devices comprises one or more feed channels, two intermediate channels branched from the feed channels and one or more drain channels connected to the intermediate channels, wherein the intermediate channels are provided with gates which can be supplied with voltage such that in the intermediate channels a substantially loop-like liquid flow results.

18. System as claimed in claim 16, wherein liquid channels are mutually connected such that a flow circulating in two liquid channels in random direction can be realized with the control means.

19. Pump system for circulating liquid, in which preferably one or more devices as claimed in any of the claims 1-14 are used, comprising:

- a liquid holder in which are provided a liquid feed channel and a liquid drain channel branched from the liquid feed channel;
- first voltage means for applying an electric field in the longitudinal direction of the liquid feed channel;
- a first and a second gate electrode which are placed on either side of the connection of the liquid drain channel to the liquid feed channel;
- second voltage means for providing the first and second gate electrode with voltage;
- control means for adjusting the first and second voltage means such that a pressure build-up occurs

at the location of said connection and the liquid is drained via the liquid drain channel.

20. Pump system as claimed in claim 19, wherein the first voltage means generate an electric field alternately in a first and in a second opposing direction in the liquid feed channel and wherein the second voltage means, substantially synchronously with the first voltage means, switch the first gate electrode into an enhancement mode and the second gate electrode into a reversement mode and vice versa.

21. Electronic circuit into which is integrated at least one device as claimed in at least one of the claims 1-14.

22. Method for manufacturing the device as claimed in any of the claims 1-14, comprising of:

- etching a channel in a wafer;
- depositing insulator material on the wafer;
- manufacturing a glass plate;
- anodic binding of the wafer on the glass plate;
- etching the wafer; and
- fixing the conductor member.

23. Method for mixing two or more liquids, comprising of:

- supplying the liquids via one or more liquid channels;
- mixing the liquids by circulating the supplied liquid, preferably in a system as claimed in claim 18;
- draining the liquids via one or more liquid drain channels.

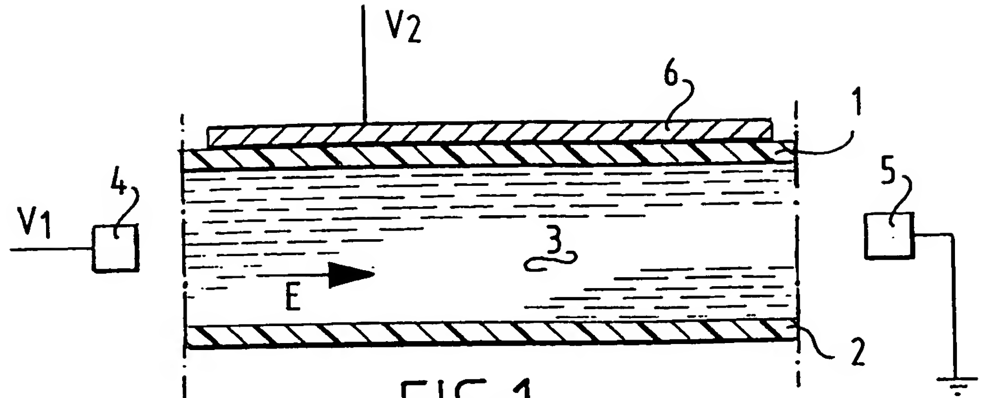


FIG.1

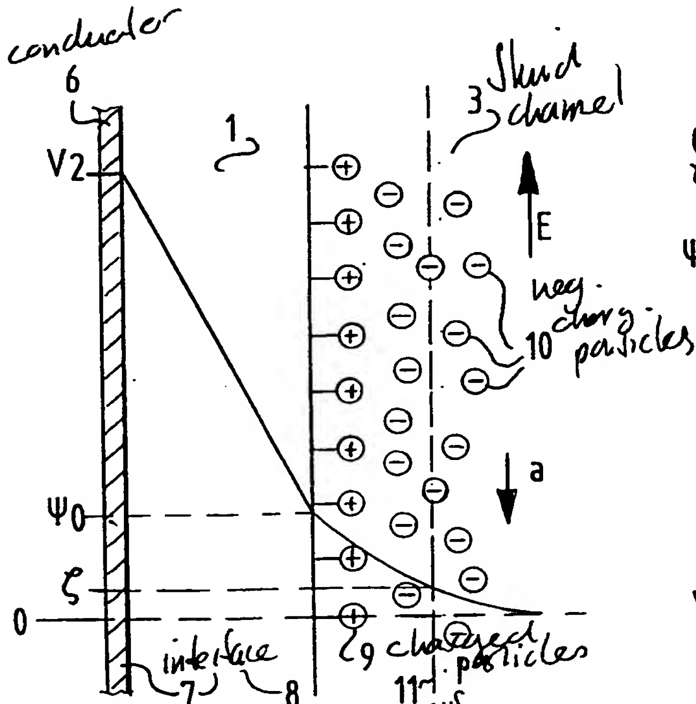


FIG.2a

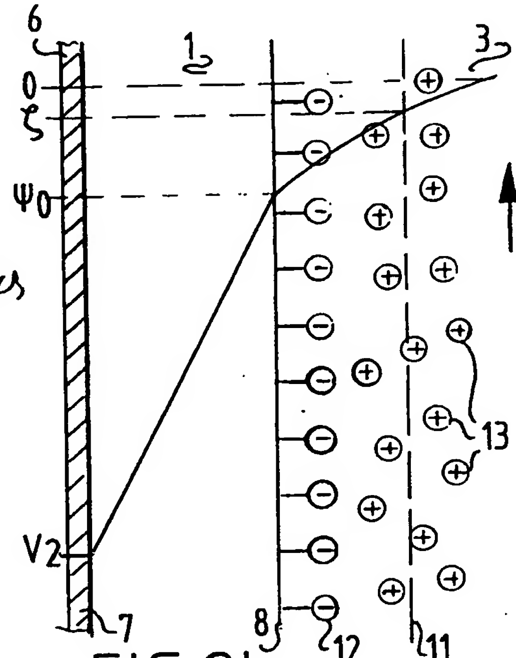


FIG.2b

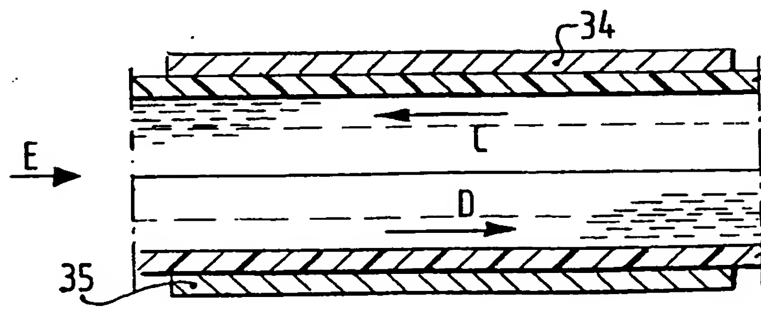


FIG.5

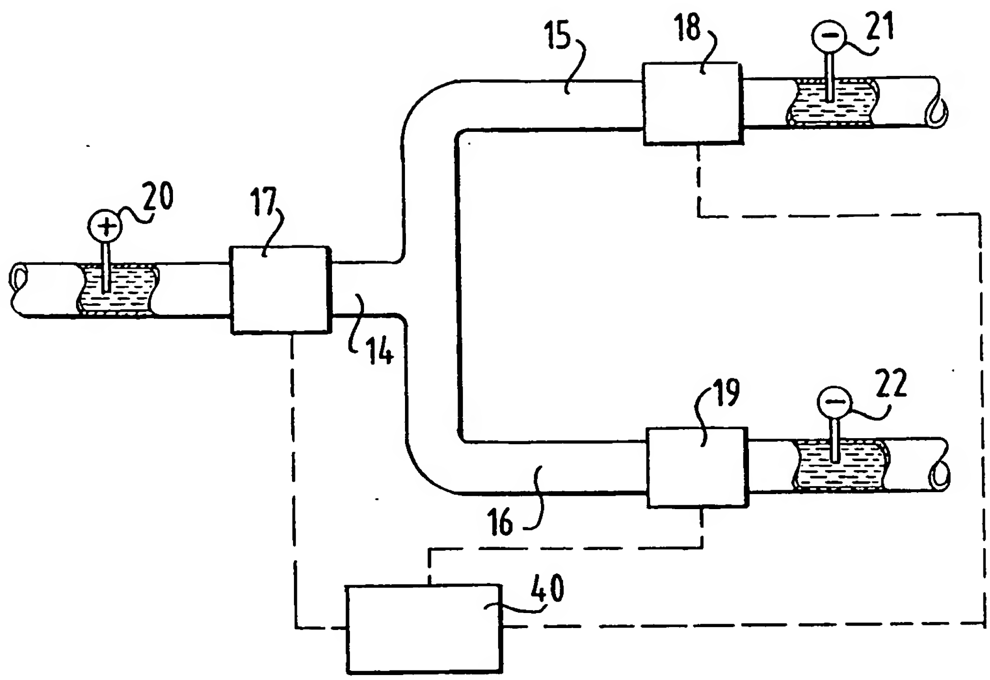


FIG.3

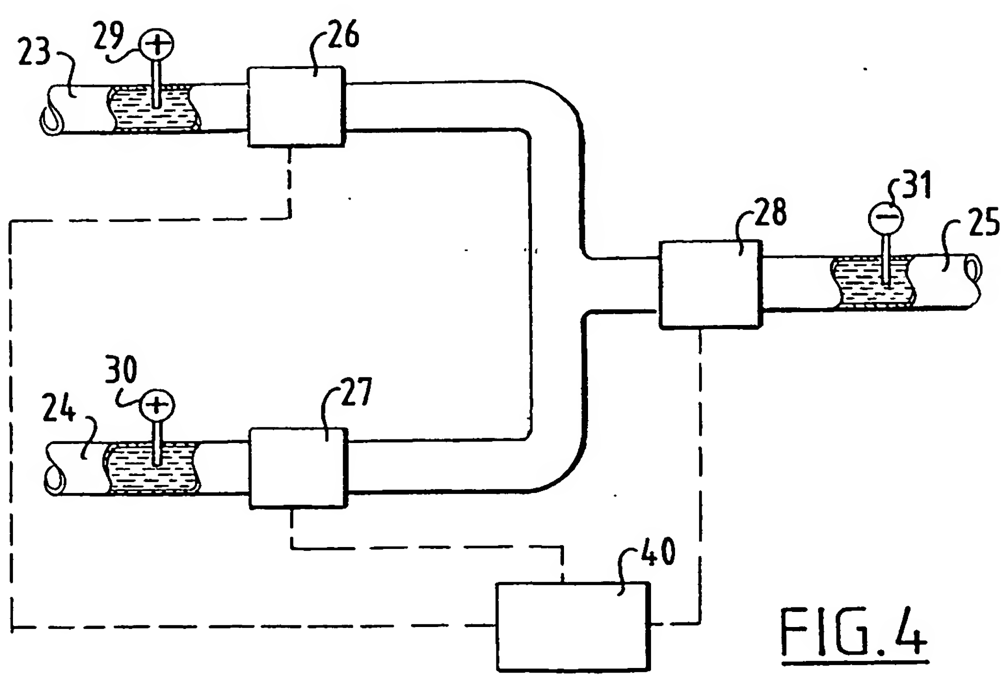


FIG.4

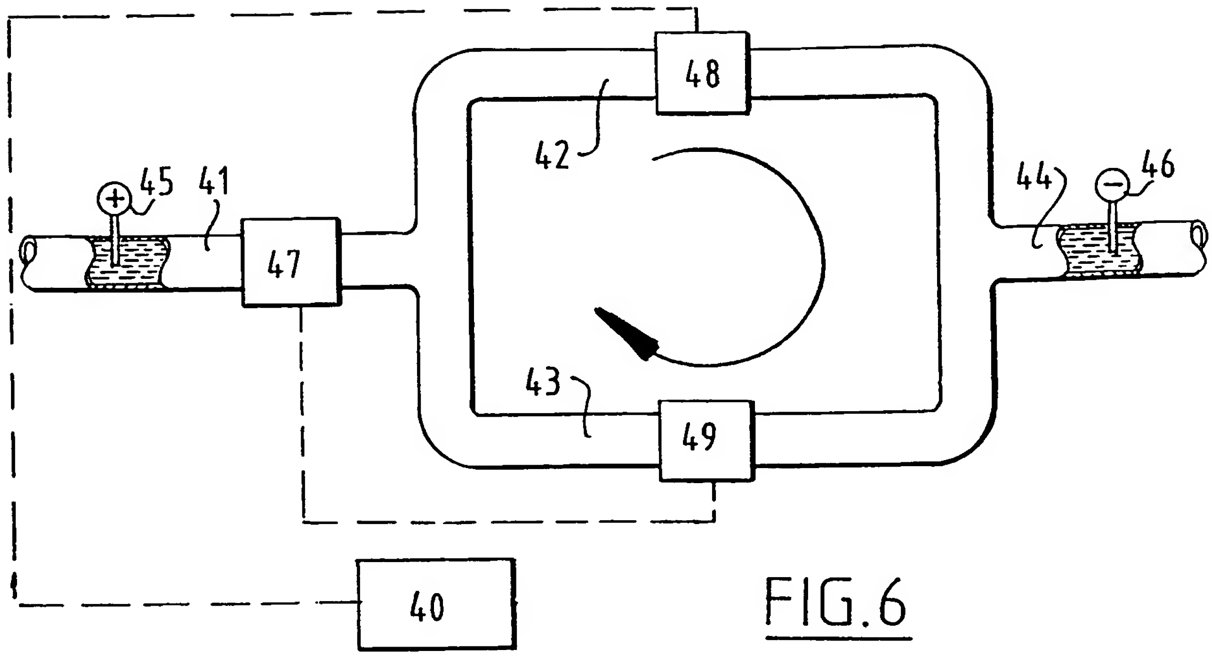


FIG.6

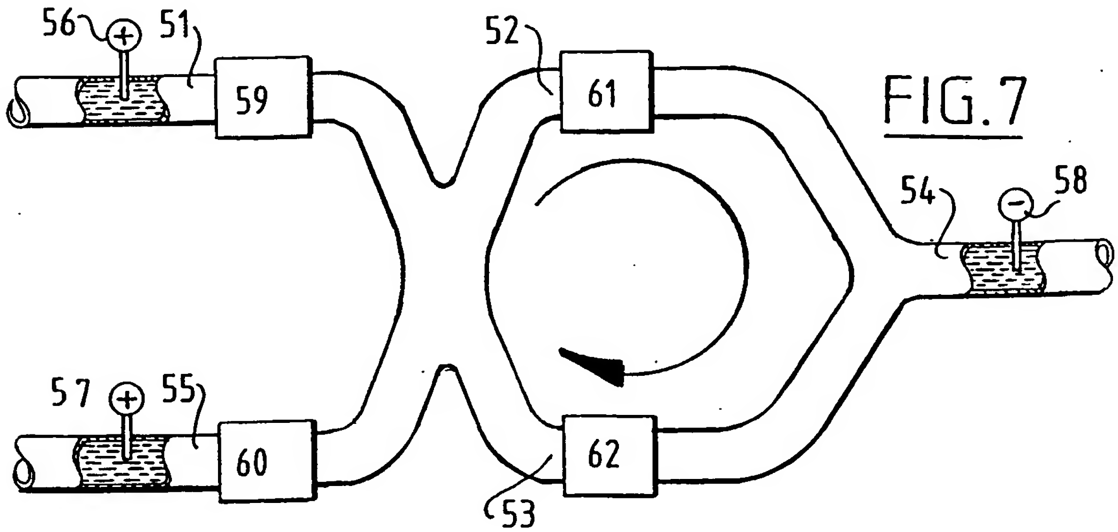


FIG.7

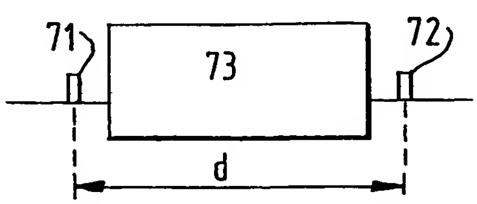


FIG.8

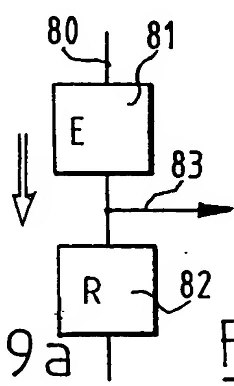


FIG.9a

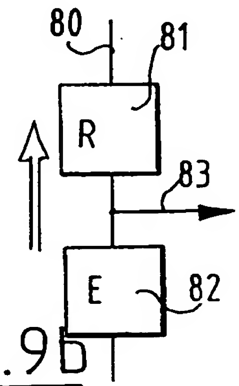


FIG.9b

INTERNATIONAL SEARCH REPORT

International Application No
PCT/NL 99/00641

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N27/447

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 092 972 A (GHOWSI KIUMARS) 3 March 1992 (1992-03-03) column 5, line 7 -column 6, line 14; figure 4	1,5,15, 19,21-23
A	US 5 374 834 A (GEIS MICHAEL W ET AL) 20 December 1994 (1994-12-20) column 6, line 33 - line 39; figure 1	1
A	WO 96 04547 A (LOCKHEED MARTIN ENERGY SYS INC ;RAMSEY J MICHAEL (US)) 15 February 1996 (1996-02-15) page 42, line 9 - line 34; figure 31	1
A	US 5 282 942 A (HERRICK STEVEN S ET AL) 1 February 1994 (1994-02-01) abstract; figures 1,2	1

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 March 2000	06/04/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Duchatellier, M

1

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 816 837 A (CALIPER TECHN CORP) 7 January 1998 (1998-01-07) column 10, line 19 - line 45; figure 4A	1
A	US 4 859 301 A (BRENNER NATHANIEL ET AL) 22 August 1989 (1989-08-22) abstract	1

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/NL 99/00641

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5092972 A	03-03-1992	NONE	
US 5374834 A	20-12-1994	US 5479035 A	26-12-1995
		US 5582701 A	10-12-1996
WO 9604547 A	15-02-1996	US 6001229 A	14-12-1999
		AU 701348 B	28-01-1999
		AU 3150895 A	04-03-1996
		CA 2196429 A	15-02-1996
		CN 1168720 A	24-12-1997
		EP 0775306 A	28-05-1997
		JP 10507516 T	21-07-1998
		US 6010607 A	04-01-2000
		US 6010608 A	04-01-2000
		US 6033546 A	07-03-2000
		US 5858195 A	12-01-1999
US 5282942 A	01-02-1994	AU 664966 B	07-12-1995
		AU 6092694 A	15-08-1994
		EP 0632890 A	11-01-1995
		JP 7505721 T	22-06-1995
		WO 9417401 A	04-08-1994
EP 0816837 A	07-01-1998	US 5800690 A	01-09-1998
		AU 3672497 A	21-01-1998
		CA 2258699 A	08-01-1998
		EP 0909386 A	21-04-1999
		WO 9800707 A	08-01-1998
		US 5965001 A	12-10-1999
US 4859301 A	22-08-1989	EP 0357255 A	07-03-1990
		JP 2032227 C	19-03-1996
		JP 2168154 A	28-06-1990
		JP 7060145 B	28-06-1995

THIS PAGE BLANK (USPTO)